

What is claimed is:

1. A method for inducing formation of new blood vessels in a mammal, wherein the method comprises administering to the mammal an effective amount of granulocyte macrophage-colony stimulating factor (GM-CSF) sufficient to form the new blood vessels in the mammal.
2. The method of claim 1, wherein the amount of the GM-CSF administered to the mammal is sufficient to increase frequency of endothelial progenitor cells (EPC) in the mammal.
3. The method of claim 2, wherein the increase in frequency of the EPC is at least about 20% as determined by a standard EPC isolation assay.
4. The method of claim 1, wherein the amount of GM-CSF administered to the mammal is sufficient to increase EPC differentiation in the mammal.
5. The method of claim 4, wherein the increase in EPC differentiation is at least about 20% as determined by a standard EPC culture assay.
6. The method of claim 1, wherein the amount of GM-CSF administered to the mammal is sufficient to increase blood vessel length in the mammal.
7. The method of claim 6, wherein the increase in blood vessel length is at least about 5% as determined by a standard blood vessel length assay.

8. The method of claim 6, wherein the amount of GM-CSF administered to the mammal is further sufficient to increase blood vessel diameter in the mammal.

5 9. The method of claim 9, wherein the increase in blood vessel diameter is at least about 5% as determined by a standard blood vessel diameter assay.

10. The method of claim 1, wherein the amount of GM-CSF administered to the mammal is sufficient to increase EPC differentiation following tissue ischemia.

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11. The method of claim 10, wherein the increase in EPC differentiation is at least about 20% as determined by a standard hindlimb ischemia assay.

12. The method of claim 1, wherein the amount of administered GM-CSF is  
15 sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.

13. The method of claim 1, wherein the amount of administered GM-CSF is sufficient to increase EPC bone marrow derived EPC incorporation into foci.

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14. The method of claim 13, wherein the increase in EPC bone marrow derived EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.

15. The method of claim 1, wherein the mammal has, is suspected of having, or will have ischemic tissue.

16. The method of claim 15, wherein the ischemic tissue is associated with an  
5 ischemic vascular disease.

17. The method of claim 15, wherein the ischemic tissue comprises tissue from a limb, graft, or organ.

18. The method of claim 15, wherein the tissue is associated with the  
10 circulatory system or the central nervous system.

19. The method of claim 15, wherein the tissue is heart or brain tissue.

20. The method of claim 1, wherein the GM-CSF is co-administered with at  
15 least one angiogenic protein.

21. The method of claim 20, wherein the angiogenic protein is an endothelial cell mitogen.

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22. The method of claim 20, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF), transforming growth factor  $\alpha$  and  $\beta$  (TGF- $\alpha$  and TGF- $\beta$ ), platelet-derived endothelial growth factor

(PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxidesynthase (NOS); or a fragment thereof.

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23. The method of claim 22, wherein the protein is one of VEGF-B, VEGF-C, VEGF-2, VEGF-3; or an effective fragment thereof.

24. A method for preventing or reducing the severity of blood vessel damage  
10 in a mammal, wherein the method comprises administering to the mammal an effective amount of granulocyte macrophage-colony stimulating factor (GM-CSF); and exposing the mammal to conditions conducive to damaging the blood vessels, the amount of GM-CSF being sufficient to prevent or reduce the severity of the blood vessel damage in the mammal.

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25. The method of claim 24, wherein the conditions conducive to the blood vessel damage are an invasive manipulation or ischemia.

26. The method of claim 25, wherein the invasive manipulation is surgery.

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27. The method of claim 25, wherein the ischemic is associated with at least one of infection, trauma, graft rejection, cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy, or myocardial ischemia.

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28. The method of claim 24, wherein the GM-CSF is administered to the

mammal at least about 12 hours before exposing the mammal to the conditions conducive to damaging the blood vessels.

29. The method of claim 28, wherein the GM-CSF is administered to the mammal between from about 1 to 10 days before exposing the mammal to the conditions conducive to damaging the blood vessels.

30. The method of claim 28, wherein the method further comprises administering the GM-CSF to the mammal following the exposure to the conditions conducive to damaging the blood vessels.

31. A method for treating ischemic tissue in a mammal in need of such treatment, wherein the method comprises:

- a) isolating endothelial progenitor cells (EPCs) from the mammal,
- b) contacting the isolated EPCs with an amount of an angiogenic protein sufficient to induce proliferation of the EPCs; and
- c) administering the proliferated EPCs to the mammal in an amount sufficient to treat the ischemic tissue.

32. The method of claim 31, wherein the EPCs have at least one of the following markers: CD34<sup>+</sup>, flk-1<sup>+</sup> or tie-2<sup>+</sup>.

33. The method of claim 31, wherein the ischemic tissue comprises injured blood vessels.

34. The method of claim 33, wherein the blood vessels are injured by an invasive manipulation.

5           35. The method of claim 34, wherein the invasive manipulation is balloon angioplasty, or deployment of a stent or catheter.

36. The method of claim 35, wherein the stent is an endovascular stent.

10           37. The method of claim 31 further comprising co-administering at least one angiogenic protein.

38. The method of claim 37, wherein the angiogenic protein is an endothelial cell mitogen or a nucleic acid encoding the endothelial cell mitogen.

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39. The method of claim 38, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF), transforming growth factor  $\alpha$  and  $\beta$  (TGF- $\alpha$  and TGF- $\beta$ ), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxidesynthase (NOS); or a fragment thereof.

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40. The method of claim 39, wherein the protein is one of VEGF-B, VEGF-C, VEGF-2, VEGF-3; or a fragment thereof.

5 41. A method for detecting presence of tissue damage in a mammal, wherein the method comprises contacting the mammal with a detectably-labeled population of endothelial progenitor cells (EPCs); and detecting the labeled cells at or near the site of the tissue damage in the mammal.

10 42. The method of claim 41, wherein the tissue damage is ischemia or an ischemic vascular disease.

15 43. A pharmaceutical product for inducing neovascularization in a mammal, wherein the product comprises isolated endothelial progenitor cells (EPCs) and is formulated to be physiologically acceptable to a mammal.

44. The pharmaceutical product of claim 43, wherein the product is sterile and further comprises at least one angiogenic protein or nucleic acid encoding the protein.

20 45. A kit for the systemic introduction of a isolated endothelial progenitor cells (EPCs), wherein the kit comprises the isolated EPCs and optionally at least one angiogenic protein or nucleic acid encoding same, the kit further optionally comprising a pharmacologically acceptable carrier solution, nucleic acid or mitogen, means for delivering the EPCs and directions for using the kit.

46. The kit of claim 45, wherein the means for delivering the EPCs is a stent, catheter or syringe.

47. A method for enhancing endothelial progenitor cell (EPC) mobilization in  
5 a mammal, wherein the method comprises administering an effective amount of at least one hematopoietic factor sufficient to enhance the EPC mobilization in the mammal.

48. The method of claim 47 further comprising co-administering to the  
mammal an effective amount of one or more of: granulocyte macrophage-colony  
10 stimulating factor (GM-CSF); at least one angiogenic protein; or an effective fragment thereof.

49. A method for inducing new blood vessel growth in myocardial tissue of a mammal in need of such treatment comprising:

15 a) injecting an effective amount of a solution comprising a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue; and

b) administering to the mammal an effective amount of at least one angiogenic factor such as stem cell factor (SCF), a colony stimulating factor (CSF) and an effective  
20 fragment thereof, thereby inducing the new blood vessel growth in the myocardial tissue of the mammal.

50. The method of claim 49, wherein the angiogenic factor is a vascular endothelial growth factor (VEGF) or an effective fragment thereof.

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51. The method of claim 50, wherein the VEGF is VEGF-1 or VEGF165.

52. The method of claim 49, further comprising expressing the angiogenic protein or fragment in the myocardium.

53. The method of claim 52, wherein the method further comprises increasing frequency of endothelial progenitor cells (EPC) in the mammal.

54. The method of claim 53, wherein the increase in frequency of the EPC is at least about 20% as determined by a standard EPC isolation assay.

55. The method of claim 49, wherein the method further comprises increasing EPC differentiation in the mammal.

56. The method of claim 55, wherein the increase in EPC differentiation is at least about 20% as determined by a standard EPC culture assay or a standard hindlimb ischemia assay.

57. The method of claim 50, wherein the level of VEGF or VEGF fragment expression is sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.

58. The method of claim 49, wherein the amount of administered angiogenic factor such as SCF, CSF or fragment is sufficient to increase EPC bone marrow derived EPC incorporation into foci.

59. The method of claim 58, wherein the increase in EPC bone marrow derived EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.

5           60. The method of claim 49, wherein the method further comprises administering at least one angiogenic protein or effective fragment thereof before or after administration of the nucleic acid to the mammal.

10           61. The method of claim 49, wherein the method further comprises administering to the mammal an anti-coagulant before, during, or after administration of the nucleic acid to the mammal.

15           62. The method of claim 61, wherein the anti-coagulant is one or more of urokinase, plasminogen activator, and heparin.

          63. The method of claim 49, wherein the nucleic acid is directly injected with a catheter or stent.

20           64. The method of claim 49, wherein the nucleic acid is inserted into a cassette operably linked to a promoter.

          65. The method of claim 49, wherein the myocardial tissue is ischemic or is associated with infarction or dysfunction.

66. The method of any one of claims 49-65, wherein the method further comprises monitoring at least one cardiac function.

5 67. The method of claim 66, wherein the monitored cardiac function is at least one of echocardiography, ventricular end-diastolic dimension (LVEDD), end-systolic dimension (LVESD), fractional shortening (FS), wall motion score index (WMSI), NOGA, cardiac angiography and LV systolic pressure (LVSP).